

## **Remarks/Arguments**

Claims 24-31 are pending. Claims 24, 29, 30 and 31 have been amended and claim 28 has been cancelled. A new claims listing is provided.

No new matter has been added by this amendment. Support for the amendments to the claims can be found in the specification and claims originally filed.

We respectfully traverse all the rejections by Examiner Yu in his communication of 12/07/2009. Arguments for this traversal are provided below on both sets of rejections.

Reconsideration and withdrawal of rejections in view of the arguments and amendment herewith is respectfully requested.

(I) Rejection of claims 24-30 under 35 U.S.C. 103(a) as being unpatentable over De Nijs (WO 01/26621 A2) in view of Maeda et al (EP 1 209 159 A2) and Jerussi (US 6,489,341 B1)

De Nijs teaches a complex orally disintegrable tablet of Mirtazapine wherein the Mirtazapine is a layer coating over non-pereils and the coated particles are encapsulated with a gastric fluid soluble coating of a polymer. This construction is unique and complex and does not allow the tablet, while disintegrable orally, to release Mirtazapine in the mouth. The De Nijs tablet formulation, with its

special construction, cannot realize the feature and function of the present invention of a orally disintegrable tablet where Mirtzapine is capable of being released in the mouth. The Examiner fails to recognize this major difference in the inventive tablet construction that has a different mode of absorptive mechanics. De Nijs teaches teach away from the present invention in both form and function.

Additionally, the examiner combines De Nijs and Maeda *et al* to make obvious to a person skilled in the art upon reading Maeda *et al* teaching of sizing of anhydrous Mirtazapine with an average particle diameter of 10-50 micron to be preferable for pharmaceuticals and determines that such a skilled person would arrive at a conclusion of using such sizing restrictions in the formulation of a dosage composition. We disagree. Maeda , with particularity, refers to this 'preferability for pharmaceuticals' as stemming from 'the high degree of purity due to the substantially freedom of lower alcohol insolubles or residual solvents' ( (Paragraph 95). Hence purity considerations. and not pharmaceutical dosage size considerations are stipulated here. Hence Maeda does not teach or suggest the use of anhydrous Mirtazapine in the preparation of a dosage form. In short, Maeda *et al* is not enabled with respect to the formulation of anhydrous Mirtazapine.

It would be obvious to a person skilled in the art that 'preferable for pharmaceuticals' would mean specifically nothing more than a desire for purity in pharmaceutical applications. People skilled in the art well

know the complexity in specifying dosage formulations. Dosage forms and their specification can be quite complex. Any effective rationalization and design of a dosage form is an unobvious experimental exercise. We believe, that upon the combining of Maeda et al with the teaching of De Nijs, a person skilled in the art would not consider the 10-50 micron sizing as a simple dosage form restriction. It requires a lot of experimentation for a person skilled in the art to prepare the orally disintegrating tablet dosage form. As a result the Maeda et al teaching cannot cure the lack of inclusion of anhydrous Mirtazapine with 90% of the particles being less than 400 microns in De Nijs as claimed by the Examiner.

Moreover, the preparation of the De Nijs dosage form is very expensive and time consuming as opposed to the simplified cost effective manufacturing process of the present invention. This simplicity evident in the present invention arises from the elimination of special coatings of the De Nijs dosage formulation. The physical construction of the De Nijs tablet is markedly different from the present invention. The De Nijs tablet has a coating on the Mirtazapine layer aimed to prevent release of Mirtazapine in the mouth. (page 3, Line 1). The present invention is simple a compressed tablet where the Mirtazapine is directly released in the mouth upon tablet disintegration. The present invention is not of the type (c) of De Nijs described on Page 5 Line 19. The Examiner has earlier restricted process claims in this application, but the process of making the product of the instant claims highlights the difference in structure and function with the De Nijs dosage formulation.

The examiner further combines Jerussi teachings of an oral tablet comprising of 20% by weight of Mirtazapine as an active agent, 50-90% by weight of a diluent and 0.5-15% by weight of a dispersing agent with the absence of De Nijs' specification of any percentages of these to make obvious the specification ranges of the present invention.

Let's look at what Jerussi relates to. Jerussi relates to a method of treating or preventing psychosis in a patient. This method comprises of administering a therapeutically effective amount of sertindole derivative. It also relates to the adjunctive administration of a second agent like Mirtazapine (but not anhydrous Mirtazapine). Table 3 in Jerussi discloses a tablet dosage form of Sertindole derivative, comprising sertindole with excipients and not anhydrous Mirtazapine. The amount of excipients required for any dosage form depends on the nature of the drug and the desired disintegration and dissolution characteristics. A person skilled in the art cannot make this determination by simple saying that a formulational success is obvious. Once again careful and substantial experimentation is needed to arrive at a useful result.

Jerussi specifically discloses the amounts of excipients for the sertindole tablet dosage formulation whereas the dosage form according to the present invention is a hard compressed orally disintegrable tablet dosage form of anhydrous Mirtazapine along with specific amount of non-effervescent excipients. The required excipients will vary both qualitatively and quantitatively based on the

characteristics of anhydrous Mirtazapine and type of dosage form more specifically orally disintegrable tablet. Jerussi simply does not suggest or teach the use of anhydrous Mirtazapine and does not teach or suggest the dissolution and disintegration characteristics of the tablets. Once again arriving at the dosage form of the present invention is not obvious from the teaching of Jerussi.

Neither do the specificational teachings of Jerussi make obvious to a person skilled in the art what the dosage form specifications of a new active ingredient like anhydrous Mirtazapine should be. Once again, it requires a lot of experimentation for such a person to prepare the orally disintegrating tablet dosage form according to the present invention comprising anhydrous Mirtazapine with very specific amount of non-effervescent excipients.

We therefore respectfully traverse this rejection of (I) with arguments made above.

(II) Rejection of claim 31 under 35 U.S.C. 103(a) as being unpatentable over De Nijs (WO 01/26621 A2) in view of Maeda et al (EP 1 209 159 A2) and Jerussi (US 6,489,341 B1) and further in view of Tam et al (US 6,495,154)

We incorporate the arguments above once more and follow it with the following addition.

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Tam et al relates to orally disintegrating tablet dosage form of Clomipramine for delaying the onset of

ejaculation. Tam discloses generically the use of Mirtazapine as one drug for combinational therapy.

De Nijs, as shown in (I), teaches away from the instant invention by teaching orally disintegrating effervescent tablets, which substantially prevent Mirtazapine from being released orally (i.e. in the mouth rather than in the gastrointestinal tract) by applying a pH dependent coating over the Mirtazapine coating of non-pareils.

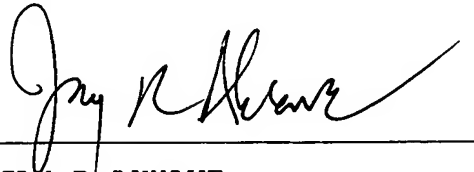
Jerussi very generically discloses the adjunctive therapy of the sertindole along with atypical antipsychotic drugs including Mirtazapine. There is no disclosure of the use of anhydrous Mirtazapine and orally disintegrating dosages thereof.

Meada et al simply discloses a process for the preparation of active ingredient anhydrous Mirtazapine of pure quality without the residual solvent and the lower alcohol insolubles. Meada et al do not teach or suggest the use of anhydrous Mirtazapine in the preparation of the dosage form.

Once again the addition of orange oil and flavorants would not be obvious to a person skilled in the art with respect to the combination of materials in the present invention comprising anhydrous Mirtazapine with specific amounts of non-effervescent excipients in view of the disclosure in De Nijs along with Meada et al, Jerussi and Tam.

We respectfully submit that the claim 31 thus is non-obvious over the combination of De Nijs, Meada et al, Jerussi and Tam et al teachings.

Respectfully submitted,

A handwritten signature in cursive script, appearing to read "Jay R Akhave", is written over a horizontal line.

JAY R AKHAVE

Reg. No. 50, 016

2058 N Mills Ave, # 612  
Claremont, CA 91711  
909-730 3492

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